REMARKS/ARGUMENTS

I. The Outstanding Rejections.

Claims 7-10 stand rejected under 35 U.S.C. §112 (first paragraph) as assertedly including new matter.

Claims 7-14 stand rejected under 35 U.S.C. §103(a) Over Godiska, U.S. 5,759,804 in view of Shen EP 0 726 310.

II. Preliminary Remarks

The present invention relates to the discovery (1) that there is a self-annealing problem with dried primers and (2) that the solution to that problem is the use of shorter dried primers. Accordingly, the invention provides methods of forming random mixtures of oligonucleotides which are resistant to self-annealing and relates to the recognition that the self-annealing problem is specific to 9-mers (and longer oligonucleotides) used in dried kits and does not represent such a problem with shorter dried primers.

As stated in Applicant's previous response, the Board of Patent Appeals and Interferences declined in the decision on appeal to reach the merits of the rejection under 35 U.S.C. §112 (first paragraph).

III. The Rejections Under 35 U.S.C. § 112 (first paragraph) Should be Withdrawn.

The new matter rejection of claims 7-10 under 35 U.S.C. § 112, first paragraph, should be withdrawn because the Examiner improperly, and contrary to the teaching of Appellants' disclosure, implies a standard of absolute inalterability with respect to the term "resistant," which is contrary to the plain meaning and usage of the word.

As stated in Applicant's Appeal Brief, "Resistance" is defined as "a force that tends to oppose or retard motion", (Webster's II New College Dictionary, Houghton Mifflin Company, New York, NY, 2001, p.943, See also The Academic Press Dictionary of Science and Technology, p. 1839 (Academic Press Inc., San Diego, CA 1992)). Thus, a time-piece which is "water resistant" is not absolutely impervious to penetration by water; rather it retards or diminishes the damaging effect of moisture.

Similarly, the primers described herein are resistant, but not impervious to self-annealing. The primers herein demonstrate a significant and unexpected retarding of self-annealing compared to the prior art primers. One of ordinary skill in the art reviewing Appellant's specification, including the acknowledged reduction in self-annealing of Appellants' primer composition, would have recognized that such was the intended meaning.

Further, The Examiner asserts (page 4-5 of the Action) that the specification does not describe "whether or not the reduction in % self-priming is due to a 'selection process' of oligonucleotides having a self-annealing resistant property or whether or not the reduction in % self-priming is due to an interaction between the random oligonucleotides or whether or not the reduction in the % of self-priming is due [sic] the sequences of the oligonucleotides."

Applicant submits that the mechanism of reduction/resistance of self-priming is not at issue in the claim and therefore the specification need not necessarily describe by what mechanism the reduction is occurring. However, the specification at page 3, lines 18-27, teaches that the self-annealing of dried 9mers is due to the property that dried 9mer oligonucleotides tend to bind to each other, i.e., self-prime, while dried 6mers do not exhibit this tendency toward self-priming. Thus, the specification teaches that the reduction and resistance in self-priming of the 6mers is due to the interaction, or lack thereof, between the dried 6mer oligonucleotides. Therefore, the application has described the method by which the 6mers are resistant to self-annealing and the rejection of the claims under 35 USC §112, first paragraph, should be withdrawn.

IV. The Rejections Under 35 U.S.C. § 103(a) Should be Withdrawn.

The application Examples demonstrate a critical and unexpected difference in self-priming activity and labeling intensity between 6-8 mers and 9-mers and there is no teaching in the art that such a difference could occur. Accordingly, the obviousness rejection under 35 U.S.C. §103(a) should be withdrawn because the art fails to teach the desirability of short primers (6-8 mers) in a dried primer system or that 6-mers to 8-mers would behave differently with respect to self-priming activity and labeling intensity than do 9-mers.

More specifically, Godiska discloses liquid 6-mers but fails to teach that the selection of 6-mers to 8-mers would be desirable or would constitute a critical range in a dried primer system. While Godiska discloses a random mixture of 6-mers and other ingredients, the Examiner acknowledges that Godiska does not teach a labeling composition in a dry state. Moreover, there is nothing in Godiska that teaches that the selection of 6-mers to 8-mers is important in either the liquid or freeze dried state to reduce self-annealing. In fact, self annealing is not mentioned at all!

In addition, Shen discloses 48-mer and 22-mer primers and fails to suggest that dried primers should be shortened or alternatively any reason why the primers of Godiska should be dried. Moreover, Shen acknowledges that "whether a particular composition will function to preserve biological activity for a particular biologically active material is not a priori predictable" (page 4, lines 36-37) and only discloses freeze-drying as an "option" (pg 5, lines 14-15).

The prior art generally taught that longer primers were preferred because longer primers have higher melting temperatures and are thus more specific. Like Godiska, Shen does not recognize the potential self-annealing problem of dried oligonucleotides used in the art at the time, and states that "it should easily be possible to include the amplification primers in the lyophilized preparation ..." Applicants were the first to recognize the detrimental sideffects of the longer dried primers (page 3, lines 18-27) and discovered that shorter dried primers were advantageous over other primers commonly used in the art.

A person of ordinary skill in the art reading Godiska and Shen would not be motivated to make the shorter dried primers of the present invention. Neither disclosure refers to the problem of self-annealing, and the art primarily was of the mindset that longer primers were more efficient due to the asserted greater hybridization in the priming reaction (see page 2-3 of the specification). Further, Shen provides a contradictory teaching in stating that one could "easily" add primers to the annealing reaction to create a functional priming kit, while also saying that whether a particular composition will maintain biological function after freeze drying is unpredictable. One of ordinary skill would not immediately understand which position on freeze-drying Shen was advocating.

Nothing in Shen and Godiska, in conjunction with the prevailing use of longer primers in the art at the time, would lead one of ordinary skill to the present invention. In

contrast, the person of ordinary skill in the art would have been motivated to modify the short wet primers of Godiska to the long dry primers of Shen, not to the short dried primers of the invention. Because the claimed invention is unobvious over what was taught by the prior art and in use by those of skill in the art at the time of Applicant's invention, the rejection of the claims under 35 U.S.C. §103(a) should be withdrawn.

V. CONCLUSION

In view of the foregoing remarks, claims 7-14 are believed to be in condition for allowance. Favorable reconsideration and allowance of the application is respectfully requested. Should the Examiner have any concerns of either form or substance she is encouraged to contact the undersigned attorney at the telephone number below.

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Respectfully submitted,

By _____

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